Rabies: Protocol for Management of Human Rabies and Management of Exposures to Animals to Prevent Human Rabies



Public Health Branch

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1. Human Rabies Case Definition

- **1.1 Laboratory Confirmed Case:** Clinical illness* and laboratory confirmation including at least one of:
 - detection of rabies virus antigen by fluorescent antibody (FA) in an appropriate clinical specimen, preferably the brain or the nerves surrounding hair follicles in the nape of the neck (i.e., nuchal skin biopsy)

OR

 isolation of rabies virus from saliva, cerebrospinal fluid (CSF), or central nervous system tissue using cell culture or laboratory animal

OR

detection of rabies virus RNA in an appropriate clinical specimen (e.g., saliva, tissue, CSF) (1).

Negative results for the above tests do not rule out rabies infection because viral material may not be detectable (e.g., early in infection). CSF frequently remains negative (1).

- **1.2 Probable Case:** Clinical illness* and at least one of:
 - demonstration of rabies-neutralizing antibody (complete neutralization) in the serum or CSF of a non-vaccinated person (1). A negative serological result does not rule out rabies as antibody

does not always develop and when it does, is frequently only detectable beginning one week following the presentation of symptoms.

OR

confirmed exposure with an appropriate incubation time.

*Rabies is an acute encephalomyelitis that almost always progresses to coma or death within 10 days after the first symptom (1).

2. Reporting and Other Requirements

2.1 Reporting of Rabies in Humans:

Laboratory:

- All positive laboratory results for rabies virus in humans are reportable to the Public Health Surveillance Unit by secure fax (204-948-3044). A phone report must be made to a Medical Officer of Health at 204-788-8666 on the same day the result is obtained, in addition to the standard surveillance reporting by fax.
- Operators of clinical/medical laboratories in Manitoba are required to submit sera from probable and confirmed human cases of rabies to Cadham Provincial Laboratory (CPL). Nape of the neck or brain specimens intended for specific rabies diagnostic testing must also be submitted to CPL. In Canada, all testing of human specimens for rabies is done at the Canadian Food Inspection Agency (CFIA) laboratory https://cnphi.canada.ca/gts/reference-diagnostic-test/5224?labld=1020.

Health Care Professional:

- Probable (clinical) cases of human rabies are reportable to the Public Health Surveillance Unit by telephone (204-788-6736) during regular hours (8:30 a.m. to 4:30 p.m.) AND by secure fax (204-948-3044) on the same day that they are identified. The Clinical Notification of Reportable Diseases and Conditions form
 - http://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0013.pdf should be used for the fax report. After hours telephone reporting is to the Medical Officer of Health on call at (204-788-8666) with a subsequent MHSU0013 faxed report.
- Adverse events following immunization should be reported by health care professional within seven days of becoming aware of the event (form available at: www.gov.mb.ca/health/publichealth/cdc/docs/aefi form.pdf
).

Regional Public Health or First Nations Inuit Health Branch:

Once the case has been referred to Regional Public Health or FNIHB, the Communicable Disease Control Investigation Form
 http://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0002.pdf should be used and returned to the Public Health Surveillance Unit by secure fax (204-948-3044).

2.2 Reporting of Rabies in Animals:

Animal Test Results:

• A person who is a veterinarian, an officer appointed under The Wildlife Act or The Provincial Parks Act, an inspector appointed or designated under The Animal Diseases Act or a wildlife biologist must report to the Chief Veterinary Office of Manitoba Agriculture at 204-470-1108 (24 hours/7 days) and Manitoba Rabies Central email: Rabies@gov.mb.ca (fax: 204-948-2190) when they become aware that an animal in Manitoba has or may have rabies. Rabies is a federally reportable disease in Canada according to the Health of Animals Act, the Health of Animals Regulations and the Reportable Diseases Regulations. All testing is facilitated by Manitoba Agriculture, and occurs at the Canadian Food Inspection Agency (CFIA) laboratory.

Animal to Human Exposures:

 A person in charge of a CFIA veterinary laboratory must report a positive or negative test result for rabies in an animal in Manitoba to Manitoba Rabies Central (MRC) (email: Rabies@gov.mb.ca) when a human contact exposure has occurred from the animal. The information is then forwarded on to the appropriate regional health authority for Public Health follow-up.

Animal to Animal Exposures:

A person in charge of a CFIA veterinary laboratory must report a positive or negative test result
for rabies in an animal in Manitoba to the joint Manitoba Agriculture/Manitoba Rabies Central
email: Rabies@gov.mb.ca when another animal has been exposed to the animal being tested
for rabies.

3. Clinical Presentation/Natural History

The initial symptoms of rabies resemble those of other systemic viral infections and may include fever, headache, malaise and disorders of the upper respiratory and gastrointestinal tracts (2). After entry into the central nervous system, the virus causes an acute, progressive encephalomyelitis that is usually fatal (3, 4). The more common, agitated (furious) form presents with the classic symptoms of hydrophobia and aerophobia (severe laryngeal or diaphragmatic spasms and a sensation of choking when attempting to drink or when air is blown in the face) with a rapidly progressing encephalitis and death (5). The paralytic form of the disease manifests in progressive flaccid paralysis, has a more protracted course, and is more difficult to diagnose (5). Differences in host immune response appear more likely to explain whether furious or paralytic rabies develops than do differences in the strains of virus that cause the natural infection (2, 6). Patients remain conscious, are often aware of the nature of their illness and are usually extremely agitated, particularly when excitation is predominant (7). Almost all cases die of the disease or its complications within a few weeks of onset (2).

4. Etiology

Rabies virus is an RNA virus of the family *Rhabdoviridae*, genus *Lyssavirus* (8). Only one of the species within the genus Lyssavirus, classical rabies virus, is present in the Americas (3). Rabies virus is labile outside a living host, and does not remain infective for long periods in the environment (9). Sunlight (ultraviolet radiation), heat, solvents, detergents, and oxidizing agents have been shown to rapidly inactivate the virus (9).

5. Epidemiology

5.1 Reservoir and Source

For Humans: Globally, over 98% of all human rabies occurs following exposures to infected dogs (10). In developing countries, monkeys are the second most common source of human rabies (11). Bats are the source of most human rabies cases in North America (5, 7).

For Animals: In Canada, 34% of reported rabies cases for 2018 were in bats, 27% in raccoons, 20% in skunks and 8% in arctic foxes (12). Rabies may occur in woodchucks or other large rodents in areas where raccoon rabies is common (8). Refer to http://www.inspection.gc.ca/english/anima/disemala/rabrag/statse.shtml for current information on rabies prevalence in Canada and http://apps.who.int/globalatlas/docs/rabies/RabnetManual_user.pdf or http://www.who.int/ith/en/ for rabies prevalence in other countries.

In 2018, Manitoba submitted 153 animal samples to the CFIA laboratory for rabies testing. The samples were taken from animals who either humans or other animals had been exposed to. Fourteen samples tested positive for rabies, and of those eight were from striped skunks, 2 from other wild animals, 2 from dogs, 1 from a bovine and 1 from another domestic animal. Refer to Appendix A for more information and: https://www.gov.mb.ca/health/publichealth/diseases/rabiessurveillance.html

5.2 Transmission

Rabies virus enters the body through wounds or by direct contact with mucosal surfaces (7). It cannot cross intact skin (7). The most common form of exposure is virus-laden saliva from a rabid animal introduced through a bite or scratch (and very rarely into a pre-existing fresh break in the skin or through intact mucous membranes) (3). Human-to-human transmission occurs almost exclusively as a result of organ or tissue transplantation (13). However, human-to-human transmission can occur in the same way as animal-to-human transmission (i.e., the virus is introduced into fresh open cuts in skin or onto mucous membranes from saliva or other potentially infectious material such as neural tissue) (13). Rabies virus can be found in saliva, tears, and nervous tissues of human rabies cases and exposure to these body fluids and tissues carries a theoretical risk of transmission (14). Airborne transmission has been demonstrated in laboratory settings and suggested in caves with heavy bat infestations (3, 5), but alternate infection routes from bats in caves cannot be ruled out (15, 16). No case of human rabies resulting from consumption of raw or cooked meat from a rabid animal has been documented (14, 17); however, individuals who slaughter rabies-infected animals and handle brain and other infected material may be at risk (17). Infectious rabies virus has never been isolated from milk of rabid cows and no documented human rabies case has been attributed to consumption of raw milk (14). Motherto-child transmission of rabies is possible, but rare, because rabies virus is not present in blood and

exposure of the baby's mucosa to natural infectious fluids and tissue seems limited (18). Based on pathobiology and epidemiology, transmission by breastfeeding is unlikely to occur, although there is a paucity of evidence (14). There is no evidence to suggest that rabies virus is transmitted in either semen or embryos, or through blood (9).

5.3 Occurrence

General: It is estimated that 59,000 human deaths are caused by rabies each year, most of which occur in rural areas of Africa and Asia (14). The paralytic form of rabies is often misdiagnosed, contributing to underreporting of rabies (19). Approximately 40% of cases are in children under 15 years of age (14). Although canine rabies is well controlled in North America, the proportion of human cases due to bat exposures is increasing (20).

Canada: Since 1924, 26 people have died of rabies in Canada: 12 in Quebec, seven in Ontario, two each in Saskatchewan, Alberta and British Columbia, and one in Nova Scotia (21, 22). The five most recent cases were reported in Quebec in 2000, British Columbia (BC) in 2003, Alberta in 2007, Ontario in 2012 and BC in 2019 (21-23). The first three of the recently reported cases were attributed to unrecognized bat exposures and the fourth to exposure outside of Canada (21). All cases were fatal (21). The most recent case of rabies and subsequent death occurred in a male in BC in July 2019 and was attributed to a bat exposure (22).

Manitoba: There have been no reported human rabies cases since reporting began in Manitoba.

5.4 Incubation Period

Highly variable but usually three to eight weeks, and very rarely as short as a few days or as long as several years (3). Length of incubation depends in part on wound severity, location in relation to nerve supply, and relative distance from the brain; the amount and variant of virus; the degree of protection provided by clothing and other factors (3).

5.5 Host Susceptibility

All mammals and only mammals are susceptible to infection; the degree of susceptibility may be influenced by some host factors (age, health, nutrition, etc.) (3). The human immune response to natural rabies infection may be insufficient to prevent disease (2).

5.6 Risk Factors for Infection

People who work in close contact with domestic or wild animals such as veterinary staff, animal control and wildlife workers, and laboratory workers who handle rabies virus are at higher risk of exposure to the virus (5). Recreational activities such as hunting and trapping animals, and cave exploration may increase risk of exposure to rabid animals (5). Children are considered at higher risk for exposure to rabies because they may be more likely to approach animals and are less likely to report bites or scratches (5). Individuals who travel to countries with endemic dog variant rabies are at increased risk of infection with rabies virus.

5.7 Period of Communicability

The length of time virus may be excreted in saliva before the development of symptoms has been determined only for domestic dogs, cats and ferrets (5). In these animals, rabies virus excretion does not generally precede symptom development by more than 10 days (5). Excretion in other animals is highly variable (3).

6. Laboratory Diagnosis in Humans

No tests are available to diagnose rabies infection in humans before the onset of clinical disease, and unless rabies-specific signs of hydrophobia or aerophobia are present, clinical diagnosis may be difficult (19). Multiple specimens (e.g., saliva, CSF, serum, skin biopsy containing hair follicles from the nape of the neck) and tests (refer to Section 1, Case Definition) are usually required for antemortem laboratory diagnosis of rabies. Brain biopsy specimens are required for postmortem diagnosis. All human specimens are routed through Cadham Provincial Laboratory (CPL). Consult with CPL (204-945-6123) to arrange specimen collection and transfer. Specimens will be forwarded by CPL to appropriate reference laboratories. Guidance for submission of human specimens for rabies testing in Canada is available at: https://cnphi.canada.ca/gts/reference-diagnostic-test/5224?labld=1020.

7. Key Investigations for Public Health Response

- Rabies immunization status of the case.
- Identification of human contacts of the case (refer to section 8.2 for contact definition and management) and determination of their rabies immunization status.
- Animal exposure and travel history of the case (e.g., previously unreported or unrecognized animal exposure). The rabies virus is more prevalent in animals in some countries than others (e.g., developing countries). Refer to http://www.inspection.gc.ca/english/anima/disemala/rabrag/statse.shtml for exposures in Canada and http://apps.who.int/globalatlas/docs/rabies/RabnetManual_user.pdf or http://www.who.int/ith/en/ for current information on rabies prevalence in animals in other countries.
- Immunization status of animal if applicable.
- Availability of animal for observation or diagnostic testing.

8. Control

8.1 Management of Human Cases

Treatment:

- Supportive. There is no effective established therapy once clinical disease develops (23).
- Consultation with Neurology, ICU and/or Infectious Diseases is strongly recommended.

Infection Control Measures:

 Routine Practices in health care. Refer to the Manitoba Health, Seniors and Active Living (MHSAL) document Routine Practices and Additional Precautions: Preventing the Transmission of Infection in Health Care available at: http://www.gov.mb.ca/health/publichealth/cdc/docs/ipc/rpap.pdf

- Contact isolation for respiratory secretions for the duration of the illness.
- Articles in contact with saliva must be cleaned and disinfected following Routine Practices.

8.2 Management of Contacts of Human Cases

- Rabies post-exposure prophylaxis (RPEP) is indicated for contacts (e.g., household, health care
 workers) who are reasonably certain they were bitten by the patient or had mucous membrane
 or non-intact skin directly exposed to potentially infectious saliva or neural tissue (13). RPEP
 consists of human rabies immune globulin (Rablg) and rabies human diploid cell vaccine
 (HDCV) or rabies purified chick embryo cell vaccine (PCECV). Routine delivery of health care
 to a patient with rabies is not an indication for RPEP (13).
- If an exposure (as described above) has occurred, follow the relevant reporting, wound management, and RPEP instructions in section 8.3 below.
- Considering that rabies is always fatal, administration of RPEP (Rablg and vaccine) as soon as
 possible after birth seems appropriate, when a child is born to a suspected or known rabid
 mother, especially since there is no contraindication for RPEP in infants (10, 18). As there is no
 bite site, Rablg should be administered in the gluteal muscle (18). Computing the necessary
 dose of Rablg can be challenging in infants with low birth weight (18).

8.3 Protocol for Management of Animal Exposures to Prevent Human Rabies

Without RPEP, the average probability of developing rabies following a bite by a rabid animal to the head is 55%, upper extremity 22%, the trunk 9% and a lower limb 12% (14).

Occurrence of Human Exposures to Rabid Animals in Manitoba: Dogs and cats account for the most human exposures to animals reported in Manitoba (24). In 2017, 3 instances of human contact with known rabies positive animals in Manitoba were reported to Manitoba Rabies Central (MRC). One incident involved a scratch from a domestic cat, one incident from handling a kitten that had been exposed to a rabies positive skunk, and the third incident involved saliva from a rabid skunk coming into contact with a mucous membrane. From January 1, 2018 through to December 31, 2018, 14 instances of human contact with known rabies positive animals in Manitoba were reported to Manitoba Rabies Central (MRC). There were 8 exposures to striped skunks, 2 exposures to dogs, 1 exposure to a cow, 1 exposure to other domestic animal and 2 exposures to other wildlife. There are also exposures to presumed rabid animals that were not captured for testing. Refer to Appendix A for epidemiology of rabies in animals in Manitoba to assist in risk assessment.

Risk Assessment After Animal Exposure:

A risk assessment should be conducted, to determine if RPEP is indicated. The assessment should consider, but is not limited to the following:

- Immunization status of the animal if applicable.
- Species of the animal.
- Prevalence of rabies in that species (refer to Appendix A).
- Prevalence of rabies in other animal species in the area (refer to Appendix A). The greatest risk for exposure to rabies virus in MB is through skunk exposure, either directly or through cross species transmission (24).
- Type of exposure (refer to "Animal Exposure Definition" below.

- Provoked versus unprovoked exposure (refer to Appendix C).
- Severity and location of exposure (e.g., large deep bite on the neck is a greater indication for RPEP compared to superficial scratch on the leg).

Refer to Table 1 and Appendix D to determine when RPEP is recommended.

Animal Exposure Definition: One or more of the following exposures to potentially infective animals:

- **Bite:** any penetration of the person's skin by the animal's teeth (13).
- **Non-bite:** a scratch or abrasion (does not have to draw blood to be considered a potential exposure to rabies virus) or when saliva or other potentially infectious material (e.g., neural tissue) of the animal is introduced into fresh, open cuts in skin or onto mucous membranes of a person (13).

NOTE: Exposure to small rodents (such as squirrels, chipmunks, rats, mice, hamsters, guinea pigs, gerbils) and lagomorphs (such as rabbits and hares) has rarely been known to transmit rabies; therefore, RPEP is rarely indicated after exposure to these animals. RPEP should only be considered if the animal was behaving very unusually or in unusual circumstances (e.g., In Saskatchewan in 2007, the CFIA did confirm rabies in a hamster that had escaped in a school that had bats and many children were exposed to the hamster). Larger rodents such as ground hogs (woodchucks) and beavers can potentially carry rabies, although it is rare in Canada. The management of exposures to these animals requires a risk assessment, which includes the frequency of rabies in these animals in the geographic area, the frequency of rabies in other animals, the type of exposure, and the circumstances of the bite including whether it was provoked or unprovoked (5). Refer to appendices.

Bat exposure:

- A bite or non-bite exposure as defined above OR there has been direct contact with a bat AND a bite, scratch or saliva exposure into a wound or mucous membrane that cannot be ruled out (25). Direct contact is defined as the bat touching or landing on a person (25). Assessment can be difficult when a bat is found in the room with a child or adult who is unable to give a reliable history (25). Factors indicating that contact may have occurred include the individual waking up crying or the presence of a new bite or scratch mark (25).
- In a child or anyone else who is unable to report an exposure due to mental incapacity (including under the influence of drugs or alcohol), any direct contact with a bat should be considered a reason for an intervention, including contact through clothes as a history to rule out a bite, scratch or mucous membrane exposure may not be reliable (25).
- Inhalation of aerosolized virus by spelunkers exploring caves inhabited by infected bats or by laboratory technicians homogenizing tissues infected with rabies virus (5). The efficacy of prophylaxis after such exposures is unknown (5).

NOTE: Indirect contact and activities with potentially rabid animals (e.g., petting or handling an animal, contact with blood, urine or feces, and contact of saliva with intact skin) are not considered exposures requiring RPEP (13). Being sprayed by a skunk is also not considered an exposure (5). Exposures to reptiles or birds are not a concern as the virus does not survive in these species. Consumption of meat

or milk from a rabid animal is strongly discouraged and should be avoided, but if it occurs, RPEP is not indicated (14).

Notes on Viability of Rabies Virus in Saliva:

- Virus is viable as long as the saliva is liquid.
- No one is known to have been exposed and infected with rabies by contact with saliva on a surface.
- Saliva with virus in it would be immediately diluted in any kind of wet environment (e.g., on wet dog just attacked by rabid animal, in water bowl/ trough) and therefore of no concern.
- Saliva outside in sun would immediately dry.
- Saliva with virus exposed on intact skin is not an exposure.
- If a dog bit a rabid animal and then came to lick the owner's hands, it would not be an exposure as the virus would have likely been diluted and/or swallowed by the dog (26).

8.31 Reporting Requirements and Responsibilities After Exposure

First Health Care Provider to see Patient:

- If a health care provider believes that a person has been exposed (e.g., bitten) to an animal or human and that there is a significant risk that rabies may have been transmitted, the health care provider must complete the Report of Suspected Rabies Exposure available at: http://www.gov.mb.ca/health/publichealth/cdc/protocol/form9.pdf to the best extent possible, and fax it immediately to the region of the exposed person's current residence (see contact details on p. 3 of the form) along with any additional information requested. If the exposure was higher risk (e.g., wild animal, refer to Table 1 and Appendix D for risk stratification), contact the appropriate regional Medical Officer of Health immediately http://www.gov.mb.ca/health/publichealth/contactlist.html. After office hours, the Medical Officer of Health on call may be contacted at 204-788-8666.
- Reporting is not required if the biting animal was:
 - o a pet gerbil, hamster, guinea pig, rat or rabbit which has never been outside of a building;
 - an apparently healthy and otherwise normally behaving mouse or squirrel that was provoked (e.g., chasing or handling/feeding);
 - without clinical symptoms of rabies and there is no evidence of a history of exposure to a rabid animal.
- Note: If the health care provider is uncertain as to whether the exposure should be referred to the Regional Health Authority/First Nations Inuit Health, consultation with Public Health is recommended. Refer to p. 3 of the form for regional public health contact information.

Medical Officer of Health or Public Health Nurse:

- Upon receiving notification of an exposure from a health care provider, the Medical Officer of Health or Public Health Nurse may if he or she believes it is possible that rabies has been transmitted, take steps to ensure the following where possible:
 - o The animal is secured alive and without injury in a safe place;

- The animal is kept securely under observation for 10 days or any longer period considered necessary in a manner that will not allow for further exposures to occur (refer to Appendix B); and
- Based on risk assessment, the MOH will determine if the animal should be sent for testing. Risk assessment and rabies related advice can be obtained during regular hours, after hours and on weekends by contacting the provincial veterinarian at Manitoba Agriculture (MBAg) 204-470-1108.
- Specimen Testing: If an animal is available for testing and a decision is made to test it for rabies, specimen collection and shipping as well as the dissemination of testing results will be coordinated centrally by rabies staff from Manitoba Health, Seniors and Active Living (MHSAL), MBAg and Sustainable Development. The MOH can call 204-470-1108 to arrange sample collection as soon as possible to avoid specimen degradation or scavenging.
- Any animal suspected of transmitting rabies to a human or another animal should be reported by the local/regional MOH or public health nurse to Manitoba Agriculture at 204-470-1108 and Manitoba Rabies Central by fax: 204-948-2190.
- It is the responsibility of the Regional Health Authority or First Nations Inuit Health Office (based on the exposed person's current address) to arrange for release of human rabies immune globulin (Rablg) and rabies human diploid cell vaccine (HDCV) or rabies purified chick embryo cell vaccine (PCECV) by a Medical Officer of Health (MOH) if RPEP is necessary. In Manitoba, release of Rablg requires MOH approval/authorization. During working hours, the regional MOH should be called http://www.gov.mb.ca/health/publichealth/contactlist.html. The after working hours contact number is 204-788-8666.
- Rabies post-exposure prophylaxis started after hours by the on-call MOH will be passed on to the appropriate region's Public Health/MOH for arrangement of follow-up doses.
- After follow-up is complete, the *Report of Suspected Rabies Exposure* should be completed and faxed to Manitoba Rabies Central 204-948-2190.

Note: If relevant, refer also to Section 8.35 *Policy for Follow-up of Exposures that Cross Jurisdictional Boundaries*.

8.32 Wound Management

- Immediate and thorough cleaning and flushing of the wound with soap and water is imperative and is probably the most effective procedure in the prevention of rabies (5). Care should be taken to clean the wound to its full depth (5). Flushing for approximately 15 minutes is suggested (5). Some guidelines also suggest the application of a virucidal agent, such as iodine-containing or alcohol solutions (5). If available, eyewash stations should be used for eye exposures (20).
- Decisions regarding the use of antibiotic prophylaxis and primary wound closure should be individualized on the basis of the exposing animal species, size and location of the wound(s) and the time interval since the bite (13).
- Suturing of wounds should be avoided when possible (5). If suturing is required, and Rablg is indicated (refer to Table 1), Rablg should be administered before closing the wound(s).
- Puncture wounds and wounds contaminated with saliva are "dirty wounds"; tetanus-diphtheria combined toxoids should be given according to the recommendations in the current Canadian Immunization Guide.

8.33 Table 1: Rabies Post-exposure Prophylaxis (RPEP) for Persons not Previously

Immunized Against Rabies (Adapted from the Canadian Immunization Guide)

Animal Species	Condition of Animal at Time of Exposure	Action			
Dog, cat or ferret	Healthy appearance and is available for 10 days observation (refer to Appendix B). Domestic pets with up-to-date vaccination are unlikely to become infected with rabies. Vaccinated animals exhibiting signs suggestive of rabies, must be evaluated by a veterinarian.	Wound management but no RPEP unless animal develops signs of rabies, then immediately give RPEP. If RPEP is given: Animal should be humanely euthanized and head submitted for testing. In consultation with public health, RPEP may be discontinued if the animal tests negative for rabies. Educate client on prevention and local risk. Animal is not available for testing*: Consider RPEP based on risk assessment and educate client on prevention and local risk. Animal is available for testing: Base RPEP decision on risk assessment. Where RPEP has been initiated and the CFIA laboratory reports a rabies negative result in the animal, the MOH will determine if the vaccine series should be continued. Educate client on prevention and local risk.			
	Rabid or suspected rabid: Higher index of suspicion if: unimmunized animal or animal with clinical symptoms consistent with rabies or unprovoked attack (refer to Appendix C) or unknown condition (e.g., escaped*).				
Wild animal (such as a fox, skunk or raccoon) and exotic pet (other than ferret)	Signs suggestive of rabies in wild animals: Unusually friendly or aggressive Nocturnal animals wandering in daylight Paralysis (27) or Other symptoms consistent with rabies	 Animal is not available for testing: Consider RPEP based on risk assessment and educate client based on local risk (Appendix A). Animal is available for testing: Base RPEP decision on risk assessment. Educate client on prevention and local risk. If RPEP has been initiated and the CFIA laboratory reports a rabies negative result in the animal, the MOH will determine if the vaccine series should be continued. 			
Bat	Signs suggestive of rabies: Flying in daytime Weakening and loss of flying ability	Bat is not available for testing: Initiate RPEP for known bites, scratches or saliva exposures into wounds or if direct contact from bat such as while the bat is in			

	Attacks a personHangs on tenaciously	 flight, as there is high prevalence of rabies in bats. Bat is available for testing: Initiate RPEP for known bites, scratches or saliva exposures into wounds. If bat tests negative for rabies, the MOH will determine if the vaccine series should be discontinued.
Livestock	Rabid horses and cattle may present with difficulty swallowing and generate copious amounts of saliva posing a greater risk for non-bite exposures.	Regardless of whether or not animal is available for testing, consult appropriate public health and provincial Chief Veterinary Office for guidance. Cattle and any livestock on pasture/rangeland are at risk of contracting rabies from wildlife.
Small rodents or lagomorphs (hares, rabbits), large rodents (woodchucks, beavers), other mammals	Consider individually. In 1999, 2 woodchucks (groundhogs) in Manitoba were found to be rabid.	Regardless of whether or not animal is available for testing, consult appropriate public health and provincial Chief Veterinary Office for guidance. Bites from squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits and hares rarely require RPEP unless the behavior of the biting animal was highly unusual (13). Biting is not unusual behavior for small rodents if they are picked up or being fed (28).

^{*}Public Health/Nursing Station should advise exposed person to obtain assistance from local animal control services in searching for the animal (in Winnipeg: Animal Services 204-986-2155 or 311; outside Winnipeg 1-877-311-4974; after hours use Police Dispatch 204-986-6222). Cats tend to be outdoors without their owner more frequently than dogs, increasing their chances of an unrecognized exposure to a rabid animal. Therefore, it is likely that the risk of acquiring rabies from an unknown/escaped cat is greater than from unknown/escaped dogs (28).

Refer to Appendix D: Human Rabies Prevention Risk Assessment Algorithm

8.34 Instructions for RPEP Administration

RPEP Administration for Previously Unimmunized Individuals

General:

- Rabies PEP should always include RabIg and rabies vaccine (HDCV or PCECV) except for
 previously immunized individuals (refer to RPEP Administration for Previously Immunized
 Individuals below). The RabIg provides immediate passive protection until the exposed person
 mounts an immune response to the rabies vaccine (5).
- When indicated (refer to Table 1 and Appendix D), RPEP should be started after the exposure and should be offered to exposed individuals regardless of the elapsed interval (5, 29).

• It should be emphasized to RPEP recipients that the current treatment only protects them against the most recent exposure and does not provide lifelong immunity. Any subsequent exposures will require evaluation to determine if another course of RPEP is warranted (30).

As rabies is a fatal disease, any contraindication to vaccine should be carefully re-considered before withholding post-exposure immunization (2005 NACI statement). **Immunization providers should consult the respective product monograph prior to administering Rablg and rabies vaccine for information such as storage and handling requirements, administration schedule, injection site, dose specific to age and weight etc. to ensure appropriate use.**

Rablg:

- The recommended dose of Rablg is 20 IU/Kg body weight for all age groups including children, given on the first day of initiation of therapy (day 0) (5). Because of possible interference of Rablg with the immune response to the rabies vaccine, the dose of Rablg should not be exceeded (5).
- The full dose of Rablg should be infiltrated into the wound and surrounding area if possible (5, 25). Any remaining volume of Rablg should be injected intramuscularly using a separate needle, at a site distant to that of vaccine administration (5, 25). Note: The World Health Organization no longer recommends injecting the remainder of the calculated Rablg dose at a distance from the wound. For bat bites or scratches, WHO recommends that Rablg be injected around the site of exposure to the degree that is anatomically feasible. For mucosal exposures with no wound, further rinsing with diluted Rablg can be considered (14).
- When more than one wound exists, each wound should be locally infiltrated with a portion of the Rablg using a separate needle (5). According to the product monograph for HyperRab Format 1 x 1 ml of 300 IU/ml, "if the wound covers a large area and the HyperRAB® dose has insufficient volume to infiltrate the entire wound, the HyperRAB® dose may be diluted with an equal volume of dextrose, 5% (D5W) in water. Do not dilute with normal saline".
- If the site of the wound is unknown, the entire dose should be administered intramuscularly at a separate site from the administration of rabies vaccine (5).
- Rabies vaccine and Rablg should never be mixed in the same syringe (5).
- If Rablg is not administered as recommended at the initiation of the rabies vaccine series, it should be administered up to and including day 7 after vaccine is initiated but should not be administered after that time (5).
- It is important to avoid the compartment syndrome which occurs if large volumes of Rablg are injected into a small body area with limited tissue (14).

Rabies Vaccine (HDCV or PCECV):

- Four 1.0 mL doses of HDCV (human diploid cell rabies vaccine) or PCECV (purified chick embryo cell rabies vaccine) should be administered intramuscularly (IM) to previously unimmunized immunocompetent persons, in addition to the Rablg discussed above (5).
- The first dose (day 0) of the four dose course of rabies vaccine should be administered as soon as possible after exposure (5). Additional doses should be administered on days 3, 7, and 14 after the first vaccination (5).
- Vaccine should be administered IM into the deltoid muscle of older children and adults or into
 the vastus lateralis muscle (anterolateral thigh) in infants, but never in the gluteal region as this
 may result in decreased response to the vaccine (5). The rabies vaccine and Rablg should be

- given at different anatomical sites on day 0, using a separate needle and syringe (5). For subsequent vaccine doses, the limb where the Rablg was administered can be used (5).
- The vaccination schedule should be adhered to as closely as possible and it is essential that all recommended doses of vaccine be administered (5). Although there is little or no evidence, in keeping with routine immunization practice, it is recommended that, if a dose of vaccine is given at less than the recommended interval, that dose should be ignored and the dose should be given at the appropriate interval from the previous dose (5). If a dose of vaccine is delayed, it should be given as soon as possible and the schedule resumed, respecting the appropriate intervals from the latest dose (5). If the vaccination schedule has been altered and there is doubt about a sufficient immune response, post-vaccination serology should be obtained 7 to 14 days after completing the vaccination series (5).
- Immunocompromised Persons: Previously unimmunized immunocompromised persons, including those taking corticosteroids or other immunosuppressive agents, and those who have immunosuppressive illnesses, and those taking chloroquine and other antimalarials, should receive a five dose regimen on days 0, 3, 7, 14 and 28 with one dose of Rablg on day 0 (5). Antibody titres should be determined 7 to 14 days after completing RPEP. If the titre is < 0.5 IU/mL, a second series of rabies vaccine should be given followed by serologic testing (5). Rablg should not be repeated. Refer to the current Canadian Immunization Guide for follow-up of immunization of immunocompromised persons https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations.html.

RPEP Administration for Previously Immunized Individuals

- Rablg is not indicated and should not be given to someone who has been previously appropriately immunized as follows:
 - Documentation at any time in the past of a complete course of pre-exposure {defined as 3 x 1.0 mL intramuscular (IM) (not in gluteal muscle due to the risk of decreased immune response) or 0.1 mL intradermal (ID) doses of rabies vaccine given on days 0, 7 and any time between days 21 to 28} or post-exposure prophylaxis with HDVC or PCECV (refer to RPEP Administration above)
 - Documentation of complete immunization with other types of rabies vaccine, or with HDCV or PCECV according to unapproved schedules, with the demonstration of an acceptable concentration of neutralizing rabies antibody in serum after completion of the series (5). An antibody titre of at least 0.5 IU/mL is considered an acceptable correlate of protection (5). Protective antibodies are present immediately after passive vaccination with Rablg and have a half-life of approximately 21 days (5).
- In previously appropriately immunized individuals who require post-exposure prophylaxis, two
 doses of HDCV or PCECV, one administered immediately and the other 3 days later, are
 recommended (5).
- A complete course of either HDCV or PCECV, as well as Rablg, is recommended for those who
 may have received rabies vaccines in the past but do not fulfill the criteria listed above for
 appropriate vaccination (5). A serum sample may be collected before the initiation of postexposure prophylaxis to test for rabies antibody, and if an acceptable antibody concentration

(0.5 IU/mL or greater) is demonstrated, the vaccine course may be discontinued, provided that at least two doses of vaccine have been given (5). If in doubt, consultation with an infectious diseases or public health physician is recommended.

8.35 Rabies Post-exposure Prophylaxis for Travelers Exposed in Another Country Where RPEP was Started

An MOH should be consulted regarding travelers who have had an exposure to a potentially rabid animal in a developing country, even if the traveler received a complete course of post-exposure prophylaxis in that country (5), in order to do an assessment of the biologicals used. The prevalence of rabies in developing countries is generally higher than in Canada, and there may be concerns about the potency of available vaccines in these countries. Options for consideration in the management of travelers exposed in developing countries include initiating or repeating all or part of the post-exposure management, obtaining post-vaccination serology, or both (5). Refer to the CATMAT rabies statement available at: http://publications.gc.ca/collections/Collection/H12-21-2-28-4.pdf and the list of rabies vaccines that meet WHO safety and efficacy requirements, available at: https://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/.

If the MOH considers the RPEP series begun in another country to be valid, but it was not completed, the series can be continued in Manitoba using a rabies vaccine that is licensed in Canada. If no Rablg was administered in the other country, Rablg should be administered only if no more than 7 days have passed since the first dose of vaccine was given (5).

If it cannot be confirmed that an efficacious vaccine was used in the other country, and if timely rabies antibody levels cannot be determined, it would be advisable to restart the rabies vaccine schedule from Day 0. If the person did not receive Rablg in the other country, or the Rablg was of questionable validity, Rablg should be given at the same time that a valid rabies vaccine series is initiated. If the Rablg was not initiated at the same time as the vaccine series, it can be given if no more than 7 days have passed since administration of the first dose of valid vaccine.

8.36 Policy for Follow-up of Exposures that Cross Jurisdictional Boundaries

Situations where more than one jurisdiction could be involved in the follow-up of animal exposures include:

- The exposed person lives in a community served by one Regional Health Authority (RHA) but the exposure occurred in a community served by another.
- The exposed person lives and was exposed in a community served by one RHA but seeks initial medical care in a community served by another.
- The exposed person lives in a First Nations community but seeks initial care in a RHA.

Policy:

Jurisdiction of current residence of exposed person (including persons exposed out-of-province or out-of-country) has ultimate responsibility for appropriate public health investigation and follow-up. Current residence is defined as where the person is living during

- the exposure follow-up period (normally between 0-38 days after exposure depending on whether prophylaxis is begun immediately, after a 10-day observation period or not at all and whether person is immunocompromised).
- Animal exposure occurs in a different jurisdiction from *current residence* (e.g., person bitten outside province, then comes home). The jurisdiction of current residence must contact the jurisdiction (or other province, country) where the exposure took place and notify it that animal exposure follow-up is required. The jurisdiction where the exposure took place must report the required follow-up information back to the jurisdiction of *current residence*.
- Responsibility when exposed person moves to a different jurisdiction during follow-up period. It is the responsibility of the exposed person to alert health care providers of any move to a different jurisdiction during the follow-up period. The jurisdiction of *current residence* that began follow-up must alert the jurisdiction (including another province or country) that the person moved to of the type of follow-up required.
- Referral of animal exposure when follow-up period is unclear. When hospitals, clinics and Health Links-Info Santé refer animal exposures for public health investigation and follow-up, the duration of the follow-up period may not always be obvious. In this case, *current residence* is defined based on location in the first 10 days following exposure.

8.4 Preventive Measures

 Corneas or organs should not be collected from a patient who died due to rabies encephalitis or any undiagnosed neurological disease (17).

8.41 Immunization

- Provide pre-exposure immunization and serological monitoring of individuals with occupations
 placing them at high risk of exposure to rabies as per the current Canadian Immunization Guide
 recommendations. Refer to the current Manitoba eligibility criteria available at:
 http://www.gov.mb.ca/health/publichealth/cdc/vaccineeligibility.html. High-risk persons should
 contact their health care provider or local public health nurse for pre-exposure immunization.
- Individuals not meeting the eligibility criteria for publicly-funded vaccine but who may be at higher risk of contact with rabid animals through recreational activities (e.g., hunters) should consult their health care provider.
- Travelers to endemic areas where there is poor access to adequate and safe post-exposure
 management should consult travel health clinics for appropriate vaccination recommendations
 (5). The cost of rabies pre-exposure immunization for travel purposes is not covered by
 Manitoba Health, Seniors and Active Living.
- Rabies post-exposure prophylaxis in individuals sustaining animal/human exposures.

8.42 Education

- Public awareness of the risk of rabies exposure through contact with a variety of animals (e.g., skunks, bats) (20). Immunization of domestic animals is highly efficacious in reducing risk of rabies.
- Informing the public on what to do if exposed to a possibly rabid animal.

8.43 Animal Management

- Register, license and immunize all dogs when feasible in enzootic countries (3).
- Immunize all cats and ferrets and other domestic animals that can be immunized (e.g., livestock).
- Sterilize pets.
- Keep pets under control (e.g., leashed), especially in unfamiliar territory or where they are more likely to encounter other domestic or wild animals.
- Identify and cover potential entrances (e.g., chimneys) for wildlife, including bats (8).
- Fill electrical and plumbing holes with stainless steel wool or caulking (25).
- Consult with animal control or wildlife professional if bats are roosting in a home (15, 25).
- Avoid contact with wild or stray animals and warn young children against such contact (30).
- Avoid and do not handle sick or strange-acting domestic and wild animals (3).
- Do not keep wild animals as pets.
- Report any strange-acting animals as well as dead animals found on residential property to the local public health unit or animal control office (30).
- Report human exposures to an animal suspected of having rabies to Health Links-Info Santé at 204-788-8200 in Winnipeg or toll-free 1-888-315-9257.
- Report domestic animals exposed to or injured by an animal suspected of having rabies (where no human exposure has occurred) to Manitoba Agriculture at 204-470-1108.
- Wear protective gloves and use shovels when removing dead animals from property (30).
- Euthanize wild animals that have bitten a person and examine the brain for evidence of rabies (3).
- Quarantine all domestic animals suspected of being exposed to a confirmed or suspected rabid domestic or wild animal.

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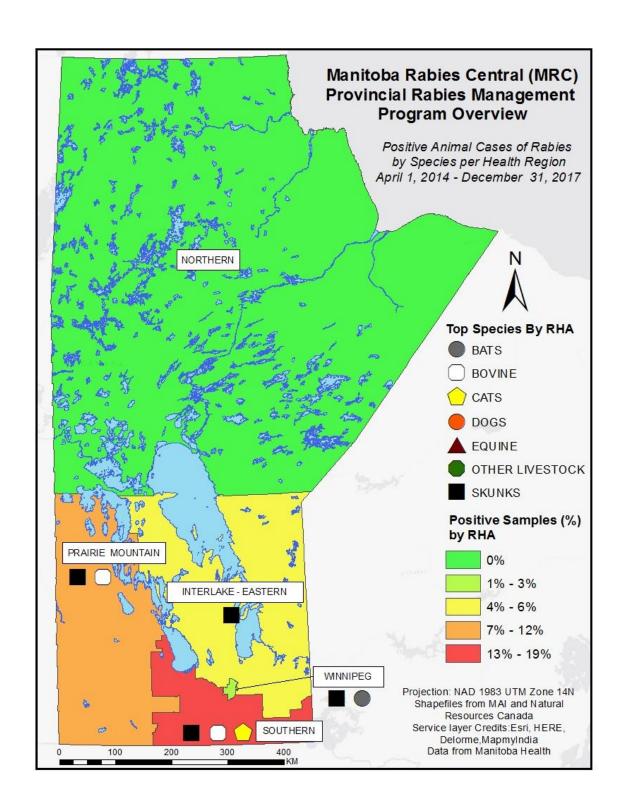
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Appendix A: Epidemiology of Rabies in Animals in Manitoba

Results on Animals Submitted for Rabies Testing in Manitoba April 1, 2014 – March 31, 2018. (by Animal)

Animal	Total Number Submitted	Percent of Total	Negative for Rabies	Positive for Rabies	Percent Positive	Rabies Result Unfit
Skunk	67	12%	27	38	57%	2
Bovine	67	13%	58	8	12%	1
Cat	134	25%	129	5	4%	0
Dog	145	28%	139	4	3%	5
Bat	24	5%	22	2	8%	6
Equine	18	3%	17	1	6%	0
Livestock	9	2%	8	1	11%	
Bear	2	0%	1	0	0%	
Raccoon	20	3%	19	0	0%	
Wolf	2	0%	2	0	0%	
Arctic Fox	3	1%	3	0	0%	
Red Fox	4	1%	4	0	0%	
Wild Animal	22	4%	21	0	0%	2
Ovine	4	1%	4	0	0%	
Coyote	6	1%	6	0	0%	
Grand Total	537	100%	460	61		16



Appendix B: 10 Day Animal Observation

In the City of Winnipeg, the Animal Services Agency may be willing to manage the animal observation period. The owner of the animal would be charged a fee for the provision of this service.

Purpose: to cover the timeframe that the possible rabies infected animal would be infectious to humans (period of communicability).

When to Initiate: Initiating a 10 day observation period of a cat or dog or a ferret before making a decision on post-exposure prophylaxis is appropriate when:

• the bite victim (or family) is confident that the owners will notify them or a veterinarian immediately, if a significant change in health or behavior of the animal occurs during this period.

Procedure: Healthy dogs, cats and ferrets will normally be confined to immediate premises (in a manner that will not allow for further exposures to occur) and observed for behaviour changes by a responsible owner for 10 days. If this option is not feasible, alternate arrangements will be made.

- If the animal does not die, appear clinically ill or display a significant change in behaviour during this period it can be concluded that the animal was not shedding rabies virus at the time of the exposure and was therefore non-infectious (3). No further public health follow-up is required.
- If the animal does display a significant change in behavior or signs of illness suggestive of rabies or dies during the observation period, the Regional Health Authority/First Nations Inuit Health must report the incident to Manitoba Agriculture at 204-470-1108 and Manitoba Rabies Central/Manitoba Agriculture email: Rabies@gov.mb.ca Fax: 204-948-2190.

Note: The observation period for an animal that has bitten a human is **not** the same as the animal quarantine period. The animal quarantine period refers to the length of time that a domestic animal/pet is isolated after it has been bitten by an animal suspected of being infectious for rabies. This period is longer (up to six months).

Appendix C: Provoked and Unprovoked Attacks

The following table can be used to distinguish provoked from unprovoked attacks in dogs; some situations may be extended to other domestic animals (e.g., beating any animal, stepping on a cat). Unprovoked dog attacks are more suggestive of rabies than provoked attacks especially where rabies is endemic. Unprovoked attacks are typically characterized by an animal crossing neutral space to attack the person. However, rabid cats and dogs may become depressed and try to hide in isolated places (27).

Provoked Attack

- 1. Entering an unfamiliar compound with a guard dog
- 2. Walking past a dog
- 3. Stepping on or bumping into a dog
- 4. Interfering in a dog fight
- 5. Taking puppies from their mother
- 6. Taking food, a toy or other possession from a dog
- 7. Playing in an area where a dog is located
- 8. Handling/surprising a dog while it is sleeping
- 9. Beating a dog
- 10. Petting or playing with a strange dog
- 11. In general, attempting to feed or handle an apparently healthy domestic animal that a person is not familiar with (3, 16).

Not Considered Provoked but may Still Result in the Animal Behaving Aggressively*

- 1. A person bitten by a dog being walked by another person.
- 2. A person bitten by another dog while walking their own dog.
- 3. A person bitten by a dog while rollerblading, skateboarding or riding a bike (28).

Unprovoked Attack

- 1. Attack by a dog for an unknown reason and from an unknown site (neutral territory).
- 2. A person bitten by their own dog that has no prior history of aggression due to known behavioural issues.

*In a geographic area that has almost no identified terrestrial rabies cases, these exposures are very likely to result from the dog's territorial or fear-aggression behavior and not aggression due to rabies (28).

Appendix D: Human Rabies Prevention Risk Assessment Algorithm

